IN THE

Supreme Court of the United States

OCTOBER TERM, 1979

No. 79-136

SIDNEY A. DIAMOND, COMMISSIONER
OF PATENTS AND TRADEMARKS,

Petitioner,

v.

ANANDA M. CHAKRABARTY

Respondent.

ON WRIT OF CERTIORARI TO THE UNITED STATES
COURT OF CUSTOMS AND PATENT APPEALS

BRIEF ON BEHALF OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, AMICUS CURIAE

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INTEREST OF AMICUS CURIAE

The American Society for Microbiology (hereinafter Society) is a not-for-profit educational and scientific organization dedicated to the promotion of scientific knowledge of microbiology and related subjects.[1] Founded in 1899 as the Society of American Bacteriologists, the

[1] This brief is filed with the consent of both parties pursuant to Rule 42 of the Supreme Court Rules and original letters of consent accompany this brief.

Society was renamed the American Society For Microbiology in 1960 because of the broadening scope of microbiology.

Today, the Society is the largest single life science organization in the United States with over 30,000 members. It embraces 16 subspecialty divisions and publishes eight scientific journals and numerous books. In addition, the Society conducts educational meetings, seminars and workshops and directs certification activities of the American Board of Medical Laboratory Immunology and of the American Board of Medical Microbiology. It is, in sum, the principal scientific organization for microbiologists in the United States.

Underlying the Society's dedication to the advancement of scientific knowledge is its commitment that science serve the public interest. In order to address scientific matters affecting the public interest, the Society has created a Board of Public and Scientific Affairs. The Board is responsible for developing positions for the Society on public policy issues.

In the area of genetic research, the Board has established a Committee on Molecular, Genetic and Systematic Microbiology with the charge to promote the adoption of sound science policies involving genetic and molecular microbiology as they affect the public interest. Six eminent microbiologists serve on this Committee, and the members are intentionally selected to achieve expertise for the Committee in areas of microbiological genetics, virology and systematic microbiology.

The activities of both the Committee and the Board are subject to governance by the Society's managing bodies, the fifteen member Council Policy Committee (Executive Committee) and the sixty member Council (Board of Directors). The Society's procedure for formulating policy

on scientific matters of public interest is designed to produce policies drafted by a Committee of experts, and monitored and coordinated by a Board responsible for serving the public interest in science.

Having adopted careful procedures for the establishment of its policies, the Society seeks to assure that significant public discussions of microbiological issues are based upon objective data. Topics such as genetic research, for example, involve sophisticated and evolving laboratory techniques that cannot be understood easily by the general public. Such topics, nevertheless, are rightly subject to searching public scrutiny and debate.

The Society has not adopted a policy with respect to the desirability of patenting microorganisms. The Society enters this case to provide basic scientific information concerning the methods by which scientists may now apply sophisticated scientific techniques to make novel microorganisms. It is particularly important for the Court to be aware that the capability of scientists to make new microorganisms through modification of genetic elements encompasses a variety of scientific techniques and that each of these techniques constitutes the deliberate intervention of man to create a novel microorganism.

I

SCIENTISTS ARE ABLE TO MODIFY GENETIC MATERIALS TO DEVELOP NOVEL MICROORGANISMS

The genetic elements of living organisms are subject to modifications which occur in nature in random and uncontrolled ways. Mutations occur in which genetic

molecules are changed as a result of cosmic rays, x-rays, ultraviolet radiation or certain chemicals. Once a mutation has occurred, the offspring of a viable new organism may exhibit the new characteristic.

Scientists have long sought techniques for controlling alterations in genetic makeup so that novel organisms may benefit mankind. Indeed, the deliberate alteration of organisms through the application of scientific knowledge is not new. Hybrids of animals and plants are created by combining donor genes to make new species. Creation of hybrids, however, has been limited to species in which fertilization or grafting techniques could be applied.

Recently, scientists have developed techniques for deliberately altering basic genetic makeup to achieve desired characteristics. Such altered genetic elements may be artifically inserted by scientists into a microorganism with the result that the recipient microorganism takes on new characteristics that it would not naturally have possessed. These characteristics then become reproduced in the normal reproduction of the microorganism.

This intentional alteration of genes to achieve a desired microorganism utilizes certain extraordinary properties of deoxyribonucleic acid (DNA). All organisms that reproduce possess a coding of information necessary for their growth and multiplication. Such coding is on chromosomes which are long filaments of DNA which is a spiral molecule in the shape of a twisted double helix.

Strands of DNA are divided into many genes which are the basic unit of inherited information for the organism. Most experiments altering the function of an organism through modification of DNA have been conducted upon single cell microorganisms. In addition to DNA in a chromosome, microorganisms may contain smaller, extrachromosomal pieces of DNA known as plasmids. Regardless of whether a

gene is in a chromosome or a plasmid, each gene is responsible for production of a specific protein thereby directing a specific function of the microorganism.

Techniques developed for altering the genetic makeup of microorganisms by introducing foreign genes are varied. Plasmids and viruses[2] habitually present in one species of microorganism, where they code for production of a particular protein, may be artifically introduced into another microorganism that normally does not carry out the same biochemical activity. The recipient strain becomes endowed with the new property and the new microorganism may be more useful than previously existing strains. Such procedure requires the scientist to identify microorganisms displaying a desired characteristic, isolate the plasmid containing the gene responsible for the characteristic, introduce the plasmid into the recipient microorganism and achieve compatability and acceptability for the plasmid within the then new microorganism. Each of these steps involves the planning and execution of sophisticated techniques to achieve a microorganism exhibiting a desired characteristic that has not been found in nature. It was this technique that was used to produce the *Pseudomonas* strain in issue here.

Other techniques are also available. Recombinant DNA technology consists of alteration of a plasmid prior to its insertion into a microorganism. Utilizing recombinant DNA technology, genes from any source may be introduced into a microorganism in order to create a strain exhibiting new characteristics.

In recombinant technology, the scientist isolates a plasmid and, using specific chemicals (restriction enzymes) cuts the plasmid at specific sites. The desired piece of genetic

[2]Viruses may be used for the techniques discussed herein. This brief will use only the term plasmids.

material is then inserted between the cut ends of the plasmid and the recombined molecule is assembled into the plasmid's characteristic circular form.

Once recombined, the plasmid can be introduced into a suitable recipient microorganism. That organism then becomes endowed with the new gene and hence a new characteristic because the protein dictated by the gene will be manufactured by that microorganism.

Of each of these steps by the scientist - isolation of the plasmid, cutting it, isolation of foreign DNA, insertion of the foreign DNA, fusion of the plasmid, selection of a suitable recipient and actual insertion - the most technically demanding is the isolation of specific foreign DNA.[3] This can be done either by the actual chemical synthesis of a gene or by the identification and purification of the gene from another organism.

To synthesize the gene, a scientist identifies the protein to be manufactured at the direction of the gene and determines the sequence of amino acids forming that protein. Knowing the genetic code — the relationship between particular amino acids and the structure of the gene itself — the scientist may then synthesize DNA that corresponds to the proper protein. Essentially, therefore, the scientist makes the gene that is then inserted into the severed plasmid and recombined for artificial introduction into a microorganism.

Alternatively, the scientist utilizes a trial and error method, cutting and recutting chromosomes to identify that portion of the chromosome - the particular gene - causing production of the protein. Once determined, the gene is

[3]To illustrate the difficulty, *E. Coli*, a standard colon bacillus, contains over 3000 genes that are chemically similar. Isolation of a gene directing a specific function may require years of work and millions of dollars.

isolated and, by the techniques described above, is introduced into a suitable recipient.

Regardless of whether recombinant DNA or other techniques are used, the scientist not only determines what gene reproduces a particular characteristic, but also chooses a recipient microorganism, identifies and isolates plasmids or genes for insertion and makes the insertion through sophisticated techniques. Success in making a new microorganism also depends upon the success of the scientist in purifying a strain, maintaining its stability with the plasmid and causing it to manufacture protein and reproduce itself. The result is a new microorganism which has not been found in nature and which has been deliberately designed and laboriously made for the benefit of man.

II

THE MANUFACTURE OF NOVEL MICROORGANISMS PROVIDES IMPORTANT BENEFITS FOR THE PUBLIC AND FOR THE EXCHANGE OF SCIENTIFIC INFORMATION

Although the benefits of application of genetic research techniques are not an issue in this case, the parties and *amici* agree that the patentability of microorganisms will affect the pace of genetic research and the exchange of scientific information. The Society, therefore, cannot simply ignore such benefits. Present and potential benefits to the public and to science are multifarious and significant. Even a condensed review of benefits suffices to place the capability of science to make new microorganisms in a rational context. Further, the Court should be aware of a specific benefit

patentability would provide for the exchange of scientific information.

A. Benefits to the Public

Utilizing the described processes, scientists are now able to produce valuable human proteins. Human hormones may be yielded in formerly unavailable quantities thereby significantly improving therapy for certain medical conditions.

For example, recombinant DNA technology has already resulted in the bacterial production of somatostatin, a hormone naturally produced in the brain. Somatostatin is important in the treatment of acromegaly—a form of gigantism—and also in the treatment of certain forms of diabetes. Through use of a new bacteria strain with a gene inserted for the expression of somatostatin, the quantity of somatostatin produced from 100 gms. of bacteria in 2 gallons of culture medium is equal to the amount previously extracted from 500,000 sheep brains.

Additionally, the possible isolation of the insulin gene and the recent announcement (*Washington Post,* Section A, page 7, Col. 1, January 17, 1980), of inducement of microorganisms to produce a duplicate of interferon[4] are important developments.

The long range benefits are even more impressive. Genetic research and application of the knowledge will lead to a fuller understanding of genetic mechanisms. Knowledge of such processes may lead to anticipating and preventing genetic disorders and diseases and to altering the genetic

[4]Interferon is a substance produced in small quantities within humans. It has been demonstrated to be effective in attacking certain viruses and may prove to be exceedingly important in fighting virus diseases. Further, it has shown some preliminary benefits in attacking cancer.

structure of plants to increase food production.

Application of this knowledge to the symbiotic nitrogen fixaton between root nodule bacteria and leguminous host plants may lead to a broader range of hosts, ultimately increasing the capability for nitrogen fixation among cereal plants. Higher crop yields at substantially lower cost would be the beneficial result of such advances.

Scientists will also learn a great deal more about mechanisms of cellular differentation whereby some of the cells of the body form skin, others form muscle or skeletal tissue, and still others aggregate to form highly specialized organs, such as the heart, lungs, spleen, pancreas, etc. Such knowledge will be useful in controlling mechanisms whereby normal cells become transformed into cancerous cells, whereby some individuals and some tissues are more susceptible to disease than others, and whereby some diseases of genetic nature are passed from parent to offspring.

B. Benefit to the Exchange of Scientific Information.

Patenting of microorganisms is likely to enhance the exchange of scientific information because patent applications must be supported by a description which permits others to reproduce, to improve and to expand upon the patented item. 35 U.S.C. §112. Microorganisms, however, cannot be produced easily based upon a written document and, consequently, may not be placed in the hands of other researchers by written description in a patent application.

For this reason, the United States Court of Customs and Patent Appeals has mandated that a prospective patent holder for a process of making a microorganism must deposit

a new microorganism in a recognized national culture depository before filing a patent application. *In re Argoudelis*, 434 F.2d 1390, 168 USPQ 99 (CCPA 1970) (United States application); *Feldman v. Aunstrup*, 517 F.2d 1351, 186 USPQ 108 (CCPA 1975) (International application)[5] The applicant must identify the depository where the microorganism culture is deposited, give the depository's accession number and provide a description of the microorganism — for example, its morphological characteristics.

In addition, under *Argoudelis* and *Aunstrup*, the applicant's agreement with the depository must provide that the microorganism will be made available to responsible persons by the depository upon the granting of the patent. Thus, upon the grant of a patent involving a new microorganism, researchers are able to obtain a sub-culture of the microorganism from the depository without payment of royalty or license fee to the patent holder.[6]

The availability of a subculture is especially important for scientific research, because actual strains are needed for experiments. Yet, it is unlikely that commercial firms will deposit newly discovered microorganism cultures in a

[5]Although these cases involve process claims, the requirement of placement in a depository would be equally applicable to claims upon an organism itself. Indeed, it should be noted that the techniques for applying genetic research will eventually become increasingly well known and process claims will, with greater frequency, be found unpatentable because they will be "obvious". *In re* Larsen, 292 F.2d 531, 130 USPOQ 209 (CCPA 1961). Thus, patenting of the microorganism itself will likely be more important than patenting of the process. See *In re* Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

[6]A license from the patent holder will be required if the microorganism is made, used or sold in a commercial sense, but not for the sole purpose of testing or conducting research with the microorganism.

recognized depository if adequate patent protection is unavailable. The absence of patenting, therefore, would preclude acquisition of strains by researchers and would inhibit the exchange of information that is vital to research.

As an example of the operation of the deposit system, cultures of the *Pseudomonas* strains at issue in this case are on deposit with the United States Department of Agriculture Northern Regional Laboratories. If the patent application is upheld, any researcher will be entitled to a subculture for use for experimental purposes. Thus, this case presents an illustration of the benefits likely to flow to genetic research from patenting.

CONCLUSION

Insertion of genes into selected microorganisms creates novel microorganisms which have not been found in nature. These techniques and the microorganisms made by them hold promise for many beneficial uses for man.

Respectfully submitted,

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